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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/720,583	11/24/2003	Moshe Bentolila	CP428	5052

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EXAMINER	
ALSTRUM ACEVEDO, JAMES HENRY	
ART UNIT	**PAPER NUMBER**
1616	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/720,583	BENTOLILA ET AL.	
	Examiner	Art Unit	
	JAMES H. ALSTRUM ACEVEDO	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 November 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7 and 10-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7 and 10-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 7 and 10-13 are pending. Applicants previously cancelled claims 1-6, 8-9, and 14. Applicants have amended claim 7. Receipt and consideration of Applicants' amended claim set and remarks/arguments submitted on November 28, 2008 are acknowledged. All rejections not explicitly maintained in the instant office action have been withdrawn per Applicants' claim amendments.

Specification

The disclosure is objected to because of the following informalities: the word "in" is misspelled in the note of Example 1 at the bottom of page 7 as "ion." **Appropriate correction is required.**

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7 and 10-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement (new matter). The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The cited claims lack literal written support for "a dissolution rate in 0.1N HCl at 37 °C of about 89% in 30 minutes." The specification in [0015] and original claim 3 state that the composition

may have a dissolution rate of more than 80% in 30 minutes, but do not state that this dissolution rate is for the claimed composition in 0.1N HCl at 37 °C. It is noted that Table 3 on page 3 provides support for a dissolution rate in 0.1N HCl at 37 °C of 89% in 30 minutes. It is also noted that the term about is defined in paragraph 20 (i.e. on page 5, 4th paragraph) as meaning ± 20% only in reference to particle size distribution (PSD).

Response to Arguments

Applicant's arguments filed 11/24/08 have been fully considered but they are not persuasive. Applicants have traversed the instant rejection by arguing that amendment of claim 7 to recite a rate in 0.1 N HCl at 37 °C of about 89% in 30 minutes. The Examiner respectfully disagrees that this claim amendment overcomes the instant rejection, because the specification does not support a dissolution rate of about 89% at the conditions cited in claim 7, but rather a dissolution rate of 89%. The numerical value of 89% is of a different scope than the numerical value of "about 89%," as currently claimed by Applicants. Thus, the claim amendment represents new matter and the instant rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue, and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 7 and 10-13 **remain rejected** under 35 U.S.C. 103(a) as being unpatentable over Heacock et al. (U.S. 2004/0048931) ("Heacock") in view of Corvari et al. (US 2003/0022940) and Rudnic et al. ("Oral Solid Dosage Forms," In *Remington's Pharmaceutical Sciences*, 18th edition, Mack Pub. Co., Easton, PA: 1990, pp 1633-1637).

Applicant Claims

Applicants claims an oral pharmaceutical composition comprising modafinil particles, colloidal silicon dioxide, crospovidone, and povidone, characterized by a

dissolution rate in 0.1 N HCl at 37 °C of about 90% in 30 minutes, wherein at least about 15% of the cumulative total of said modafinil particles have a diameter of more than about 200 microns and more than about 5% of the cumulative total of said modafinil particles have a diameter more than about 250 microns.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The teachings of Heacock were set forth on pages 7-10 of the office action mailed on May 17, 2006 and are repeated herein. Heacock teaches pharmaceutical compositions comprising modafinil in the form of particles of defined size (abstract). These compositions may comprise particles selected from discrete lots; including a small particle size lots (sizes ranging from less than or equal to 0.1 microns to less than or equal to 200 microns), large particle size lots (sizes ranging from less than or equal to 220 microns to less than or equal to 400 microns), and very large particle size lots (sizes ranging from less than or equal to 400 microns to less than or equal to 500 microns) [0029] through [0031]. Compositions comprising different sized modafinil particles are taught in Examples 3-42 and tabulated in column 9, including compositions comprising particles wherein (a) **20% of the particles have a size of equal to or less than 200 microns** (Ex. 9) and (b**) 0-5% of the particles have a size less than or equal to 400 microns** (Ex. 11).

Heacock notes that **routine experimentation is desirable to determine optimum particle size makeup and proportions or mixtures that *exhibit similar dissolution profiles* and/or are bioequivalent to commercially available modafinil associated with the PROVIGIL®** trademark [0064].

Heacock also teaches that the compositions may further comprise surfactants, including non-ionic, ionic, and bile salt surfactants such as sodium alkyl sulfates (ionic), polyoxyethylene sorbitan fatty esters (non-ionic), and deoxycholic acid (bile salt) [0066]. The term "surfactant" reads on the term "dissolution modifier," per Applicant's description of what constitutes a dissolution modifier on page 3 of the instant specification. Heacock's invented modafinil compositions are preferably administered orally in the form of vehicles such as tablets, capsules, powders, pills, etc. [0069].

Specifically, Heacock teaches compositions with suitable modafinil particle sizes, such as compositions comprising different sized modafinil particles (see, for example, Examples 3-42, the table in column 9, including compositions comprising particles wherein (a) **20% of the particles have a size of equal to or less than 200 microns** (Ex. 9) and (b**) 0-5% of the particles have a size less than or equal to 400 microns** (Ex. 11)).

Corvari teaches novel pharmaceutical formulations comprising modafinil and one or more diluents, disintegrants, binders, and lubricants, as well as processes for the preparation of said formulations (title, abstract). Excipients are selected to ensure the delivery of a consistent amount of modafinil in a convenient dosage form and to optimize the cost, ease, and reliability of the manufacturing process. Excipients used in solid oral formulations commonly include, **diluents, binders, disintegrants, lubricants, glidants, surface-active agents**, etc. [0020]. The most common diluent is lactose [0021]. Disintegrants include **cross-linked polyvinylpyrrolidone (e.g. crospovidone NF**) and are included to facilitate dissolution and enhance bioavailability [0023]. A preferred binder includes polyvinyl pyrrolidone, in particular, **povidone** [0024]. Binders are used

as wet granulation excipients to agglomerate the active ingredient, to improve powder flow, to improve compactibility [0024]. Lubricants are used in tablet formulation to prevent sticking of the tablet to punch faces and to reduce friction during the compression stages. Suitable lubricants include salts of stearic acid, such as sodium stearyl fumarate [0025]. The formulations may comprise dosages of 10, 25, 50, and **100 mg of modafinil** in a 250 mg tablet; **200 mg of modafinil** in a 500 mg tablet; 300 mg of modafinil in a 750 mg tablet; and 400 mg of modafinil in a 1,000 mg tablet [0030]. Corvari's method of preparing the invented formulations includes the preparation of tablets, wherein the composition in one step is formed into a dried granulation mixture ([0031]-[0044]). The dried granulation mixture may also be screened to select the desired granule size [0042]. Tablets made by Corvari's process preferably have properties similar to those of PROVIGIL®.

Rudnic teaches that drug substances most frequently are administered orally by means of solid dosage forms, such as tablets and capsules (pg. 1633, left column). In addition to the active ingredient tablets contain a number of inert materials (i.e. excipients or additives) to impart satisfactory processing and compression characteristics to the formulation (e.g. diluents, binders, glidants, and lubricants) or to give additional desirable physical characteristics to the finished tablet (e.g. disintegrants) (pg. 1635, left column). Diluents include lactose (pg. 1635, left column). Binders include lactose, **polyvinyl pyrrolidone**, etc. (pg. 1635, right column). Lubricants prevent adhesion of tablet materials to the surfaces of dies and punches, reduce interparticle friction, facilitate the ejection of tablets from the die cavity, and may improve the rate of flow of the tablet granulation (pg. 1636, right column). Commonly used lubricants include talc,

magnesium stearate, stearic acid, calcium stearate, etc. Glidants are substances that improve the flow characteristics of a powder mixture and **the most commonly used glidant is colloidal silicon dioxide** (pg. 1637, left column). Asbestos-free talc is also used as a glidant and may serve the dual purpose of lubricant/glidant (pg. 1637, left column).

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Heacock lacks the teaching of modafinil composition comprising colloidal silicon dioxide, crospovidone, and povidone. This deficiency is cured by the teachings of Corvari and Rudnic. Rudnic was provided to demonstrate that colloidal silicon dioxide is a conventional excipient used in oral pharmaceutical formulations.

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been prima facie obvious to a person of ordinary skill in the art at the time of the instant invention to combine the teachings of Heacock, Corvari, and Rudnic, because Heacock teaches that pharmaceutical formulation of modafinil are most preferably administered orally in the form of a vehicle such as a tablet, which may comprise a pharmaceutically acceptable carrier that may comprise agents to aid solubility, absorption, flavor, color or texture of the vehicle or its contents ([0059], [0060], and [0068]). Examples of suitable carrier material agents taught by Heacock in [0060] include excipients, diluents, binders, disintegrating agents, lubricants, etc. An ordinary skilled artisan would have been motivated to combine the teachings of Heacock and Corvari, because both references are in the same field of endeavor and strive to

achieve a similar goal: formulations having properties similar to those of PROVIGIL®. An ordinary skilled artisan would have been motivated to combine the teachings of Heacock and Corvari, because both references teach oral pharmaceutical modafinil compositions in the form of tablets, comprising additional additives/excipients, and having properties similar to those of PROVIGIL®. It would have been obvious to combine the teachings of Rudnic with those of Heacock and Corvari, because Corvari teaches that modafinil may comprise glidants, and Rudnic identifies suitable glidants, such as colloidal silicon dioxide, which is the most commonly used glidant. Due to the aforementioned similarities an ordinary skilled artisan would have had a reasonable expectation of success upon modification of Heacock's teachings with the combined teachings of Corvari and Rudnic. Applicants' data have been noted. Applicants claim no unexpected or surprising results in the instant specification.

Response to Arguments

Applicant's arguments filed 11/28/08 have been fully considered but they are not persuasive. Applicants have traversed the instant rejection by arguing (1) there is allegedly no reason why an ordinary skilled artisan would have selected to add colloidal silicon as a glidant to Heacock's formulation; (2) Heacock allegedly lacks the teaching or suggestion of a composition comprising modafinil, wherein at least 15% of the cumulative total of said modafinil particles have a diameter of more than about 200 microns and more than about 5% of the cumulative total of said modafinil particles have a diameter more than about 250 microns; and (3) the cited prior art allegedly fails to provide any suggestion/motivation to obtain compositions having the recited particle size

distribution, because the "disclosed range is so broad as to encompass a very large number of possible distinct compositions".

The Examiner respectfully disagrees with Applicants' arguments in part. Regarding (2)-(3), Applicants are correct that Heacock does not explicitly teach compositions wherein at least 15% of the cumulative total of said modafinil particles have a diameter of more than about 200 microns and more than about 5% of the cumulative total of said modafinil particles have a diameter more than about 250 microns. However, Applicants are directed to Heacock's teachings stating:

"Routine experimentation is desirable to determine optimum particle size makeup and proportions or mixtures that *exhibit similar dissolution profiles* and/or are bioequivalent to commercially available modafinil associated with the PROVIGIL® [0064]."

Thus, an ordinary skilled artisan would have been motivated to optimize the particle size distribution of the compositions resulting from the combined prior art, per the teachings of Heacock. It is also noted that the term "about" is defined in Applicants' specification in paragraph [0020] to mean ± 20% in reference to the percentage stated and ± 10% of the stated particle size. A fair reading of Applicants' claims is that at least about 0-35% of the particles have a size of more than 180-220 microns and more than 0-25% of the cumulative total of said modafinil particles have a diameter more than 225-275 microns. Based on Applicants' definition of the term about, Applicants' claims include embodiments wherein 0% of the particles have a size of about 220 microns and wherein 0% of the cumulative total of said modafinil particles have a diameter of more than 225 microns. As a result of Applicants' definition of about and the aforementioned

discussion, it is clear that the ranges of particle sizes taught by Heacock overlap with the ranges recited in Applicants' claims. Thus, there is ample motivation in the prior art to obtain a modafinil composition exhibiting the recited particle size distribution and particle sizes.

Regarding (1), Corvari teaches that glidants are suitable excipients for inclusion in modafinil tablet formulations. Colloidal silicon dioxide is the most common glidant (Rudnic). When selecting a glidant for incorporation in Heacock's formulation as suggested by Corvari, it would have been prima facie obvious to select colloidal silicon dioxide, because colloidal silicon dioxide is the most common glidant. An ordinary skilled artisan would have had a reasonable expectation of successfully preparing a suitable modafinil formulation comprising silicon dioxide as the glidant, because it is a conventional glidant incorporated in tablet formulations.

Applicants' data is also noted. Applicants' data cannot be relied upon to overcome the instant rejection, because it is unclear to which batch prepared in Applicants' Example 1 (see Table 2 of Example 1 on page 7) correlates to the data depicted in Applicants' tables 3 and 4 (see pages 9 and 10, respectively). Table 2 in Example 1 has four different batches numbered A through D, characterized by different particle size distributions. It is also noted that the description of the particle size distributions in Table 2 does not allow one to evaluate the different batches or ascertain which batches are characterized by the particle size distribution described in Applicants' claims (e.g. it is unclear whether one batch or all batches in Table 2 are characterized by more than about 5% of the cumulative total of said modafinil particles having a diameter of more than about 250 microns). If Applicants claimed unexpected results as a reason

why the instantly claimed compositions are unobvious, it is necessary to set forth on the record, which bath (i.e. which particular particle size distribution) was used to collect the data depicted in Tables 3 and 4. Applicants' data does not overcome the instant rejection. Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because the combined teachings of the prior art is fairly suggestive of the claimed invention.

Conclusion

Claims 7 and 10-13 are rejected. No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571) 272-5548. The examiner is on a flexible schedule, but can normally be reached on M-F ~10am~5:30 pm, and Saturdays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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